

## SEQUENCE LISTING

<110 > FORSSMANN, WOLF-GEORG MAGERT, HANS-JURGEN STANDKER, LUDGER KREUZTMANN, PETER

<120> SERINE PROTEINASE INHIBITORS

<130> 10496/P65678US0

<140> 09/582,328

<141> 2000-07-19

<150> PCT/EP98/08424

<151> 1998-12-23

<150> DE 197 57 572.2

<151> 1997-12-23

<160> 41

<170> PatentIn Ver. 2.1

<210> 1

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<213> Unknown Organism

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Met Lys Ile Ala Thr Val Ser Val Leu Leu Pro Leu Ala Leu Cys Leu 1 5 10 15

Ile Gln Asp Ala Ala Ser Lys Asn Glu Asp Gln Glu Met Cys His Glu 20 25 30

Phe Gln Ala Phe Met Lys Asn Gly Lys Leu Phe Cys Pro Gln Asp Lys 35 40 45

Lys Phe Phe Gln Ser Leu Asp Gly Ile Met Phe Ile Asn Lys Cys Ala 50 60

Thr Cys Lys Met Ile Leu Glu Lys Glu Ala Lys Ser Gln Lys Arg Ala 65 70 75 80

Arg His Leu Ala Arg Ala Pro Lys Ala Thr Ala Pro Thr Glu Leu Asn 85 90 95

Cys Asp Asp Phe Lys Lys Gly Glu Arg Asp Gly Asp Phe Ile Cys Pro 100 105 110

Asp Tyr Tyr Glu Ala Val Cys Gly Thr Asp Gly Lys Thr Tyr Asp Asn 115 120 125 Arg Cys Ala Leu Cys Ala Glu Asn Ala Lys Thr Gly Ser Gln Ile Gly 130 135 140

Val Lys Ser Glu Gly Glu Cys Lys Ser Ser Asn Pro Glu Gln Val Arg 145 150 155 160

Ser Ile Val Ser Leu Met Gly Asn Thr Gly Arg Leu Thr Ser Asn Ser 165 170 175

Lys

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Ile Gln Asp Ala Ala Ser Lys Asn Glu Asp Gln Glu Met Cys His Glu 20 25 30

Phe Gln Ala Phe Met Lys Asn Gly Lys Leu Phe Cys Pro Gln Asp Lys 35 40 45

Lys Phe Phe Gln Ser Leu Asp Gly Ile Met Phe Ile Asn Lys Cys Al. 50 60

Thr Cys Lys Met Ile Leu Glu Lys Glu Ala Lys Ser Gln Lys Arg Ala
65 70 75 80

Arg His Leu Ala Arg Ala Pro Lys Ala Thr Ala Pro Thr Glu Leu Asn

Cys Asp Asp Phe Lys Lys Gly Glu Arg Asp Gly Asp Phe Ile Cys Pro 100 105 110

Asp Tyr Tyr Glu Ala Val Cys Gly Thr Asp Gly Lys Thr Tyr Asp Asn 115 120 125

Arg Cys Ala Leu Cys Ala Glu Asn Ala Lys Thr Gly Ser Gln Ile Gly 130 135 140

Val Lys Ser Glu Gly Glu Cys Lys Ser Ser Asn Pro Glu Gln Asp Val 145 150 155 160

Cys Ser Ala Phe Arg Pro Phe Val Arg Asn Gly Arg Leu Gly Cys Thr 165 170 175

Arg Glu Asn Asp Pro Val Leu Gly Pro Asp Gly Lys Thr His Gly Asn 180 185 190

d trail Lys Cys Ala Met Cys Ala Glu Leu Phe Leu Lys Glu Ala Glu Asn Ala 200 Lys Arg Glu Gly Glu Thr Arg Ile Arg Arg Asn Ala Glu Lys Asp Phe Cys Lys Glu Tyr Glu Lys Gln Val Arg Asn Gly Arg Leu Phe Cys Thr Arg Glu Ser Asp Pro Val Arg Gly Pro Asp Gly Arg Met His Gly Asn 250 Lys Cys Ala Leu Cys Ala Glu Ile Phe Lys Arg Arg Phe Ser Glu Glu Asn Ser Lys Thr Asp Gln Asn Leu Gly Lys Ala Glu Glu Lys Thr Lys 280 Val Lys Arg Glu Ile Val Lys Leu Cys Ser Gln Tyr Gln Asn Gln Ala Lys Asn Gly Ile Leu Phe Cys Thr Arg Glu Asn Asp Pro Ile Arg Gly 310 315 Pro Asp Gly Lys Met His Gly Asn Leu Cys Ser Met Cys Gln Val Tyr 330 Phe Gln Ala Glu Asn Glu Glu Lys Lys Lys Ala Glu Ala Arg Ala Arg Asn Lys Arg Glu Ser Gly Lys Ala Thr Ser Tyr Ala Glu Leu Cys Asn 360 Glu Tyr Arg Lys Leu Val Arg Asn Gly Lys Leu Ala Cys Thr Arg Glu 375 Asn Asp Pro Ile Gln Gly Pro Asp Gly Lys Val His Gly Asn Thr Cys 395 Ser Met Cys Glu Val Phe Phe Gln Ala Glu Glu Glu Lys Lys 405 410 Lys Glu Gly Glu Ser Arg Asn Lys Arg Gln Ser Lys Ser Thr Ala Ser 425 Phe Glu Glu Leu Cys Ser Glu Tyr Arg Lys Ser Arg Lys Asn Gly Arg 435 440 Leu Phe Cys Thr Arg Glu Asn Asp Pro Ile Gln Gly Pro Asp Gly Lys 455 Met His Gly Asn Thr Cys Ser Met Cys Glu Ala Phe Phe Gln Glu Glu 465 470 Glu Arg Ala Arg Ala Lys Ala Lys Arg Glu Ala Ala Lys Glu Ile Cys 490 485

3' Kn Ser Glu Phe Arg Asp Gln Val Arg Asn Gly Thr Leu Ile Cys Thr Arg 505 Glu His Asn Pro Val Arg Gly Pro Asp Gly Lys Met His Gly Asn Lys 520 Cys Ala Met Cys Ala Ser Val Phe Lys Leu Glu Glu Glu Lys Lys Asn Asp Lys Glu Glu Lys Gly Lys Val Glu Ala Glu Lys Val Lys Arg Glu Ala Val Gln Glu Leu Cys Ser Glu Tyr Arg His Tyr Val Arg Asn 570 Gly Arg Leu Pro Cys Thr Arg Glu Asn Asp Pro Ile Glu Gly Leu Asp 585 Gly Lys Ile His Gly Asn Thr Cys Ser Met Cys Glu Ala Phe Phe Gln 600 Gln Glu Ala Lys Glu Lys Glu Arg Ala Glu Pro Arg Ala Lys Val Lys 615 Arg Glu Ala Glu Lys Glu Thr Cys Asp Glu Phe Arg Arg Leu Leu Gln 635 Asn Gly Lys Leu Phe Cys Thr Arg Glu Asn Asp Pro Val Arg Gly Pro 650 Asp Gly Lys Thr His Gly Asn Lys Cys Ala Met Cys Lys Ala Val Phe 665 Gln Lys Glu Asn Glu Glu Arg Lys Arg Lys Glu Glu Asp Gln Arg 680 Asn Ala Ala Gly His Gly Ser Ser Gly Gly Gly Gly Asn Thr Gln 695 Asp Glu Cys Ala Glu Tyr Arg Glu Gln Met Lys Asn Gly Arg Leu Ser Cys Thr Arg Glu Ser Asp Pro Val Arg Asp Ala Asp Gly Lys Ser Tyr 730 Asn Asn Gln Cys Thr Met Cys Lys Ala Lys Leu Glu Arg Glu Ala Glu 740 Arg Lys Asn Glu Tyr Ser Arg Ser Arg Ser Asn Gly Thr Gly Ser Glu 760 Ser Gly Lys Asp Thr Cys Asp Glu Phe Arg Ser Gln Met Lys Asn Gly Lys Leu Ile Cys Thr Arg Glu Ser Asp Pro Val Arg Gly Pro Asp Gly 795 790

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Glu Ala Ala Glu Lys Lys Arg Lys Arg Met Lys Thr Gly Ala Ile Gln \$820\$ \$825 \$830

Glu Lys Gly Ala Ile Gln Glu Lys Gly Ala Met Thr Lys Arg Ile Cys 835 840 845

Val Val Asn Phe Glu Ala Cys Arg Glu Met Glu Ser Leu Ser Ala Pro 850 855 860

Glu Lys Ile Thr Leu Phe Glu Ala His Met Ala Arg Cys Thr Ser Ile 865 870 875 880

Asn Val Leu Cys Val Arg Ala Ser Leu Ile Glu Lys Leu Met Lys Glu 885 890 895

Lys Arg Lys Met Lys Arg Asn Gln Val Ala Ser Pro Gln Ile Met Gln 900 905 910

Arg Met Ser Ala Val Asn Phe Glu Thr Ile 915 920

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Asn Gly Lys Leu Phe Cys Pro Gln Asp Lys Lys Phe Phe Gln Ser Leu 20 25 30

Asp Gly Ile Met Phe Ile Asn Lys Cys Ala Thr Cys Lys Met Ile Leu 35 40 45

Glu Lys Glu Ala Lys Ser Gln
50 55

<210> 4

<211> 68

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Lys Leu Val Arg Asn Gly Lys Leu Ala Cys Thr Arg Glu Asn Asp Pro
Ile Gln Gly Pro Asp Gly Lys Val His Gly Asn Thr Cys Ser Met Cys
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Glu Val Phe Phe Gln Ala Glu Glu Glu Lys Lys Lys Glu Gly
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Glu Ser Arg Asn
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                                               Met Lys Ile Ala
aca gtg tca gtg ctt ctg ccc ttg gct ctt tgc ctc ata caa gat gct
Thr Val Ser Val Leu Leu Pro Leu Ala Leu Cys Leu Ile Gln Asp Ala
                     10
gcc agt aag aat gaa gat cag gaa atg tgc cat gaa ttt cag gca ttt
Ala Ser Lys Asn Glu Asp Gln Glu Met Cys His Glu Phe Gln Ala Phe
                                     3.0
atg aaa aat gga aaa ctg ttc tgt ccc cag gat aag aaa ttt ttt caa
                                                                   198
Met Lys Asn Gly Lys Leu Phe Cys Pro Gln Asp Lys Lys Phe Phe Gln
            40
                                 45
agt ctt gat gga ata atg ttc atc aat aaa tgt gcc acg tgc aaa atg
                                                                   246
Ser Leu Asp Gly Ile Met Phe Ile Asn Lys Cys Ala Thr Cys Lys Met
                             60
ata ctg gaa aaa gaa gca aaa tca cag aag agg gcc agg cat tta gca
Ile Leu Glu Lys Glu Ala Lys Ser Gln Lys Arg Ala Arg His Leu Ala
aga gct ccc aag gct act gcc cca aca gag ctg aat tgt gat gat ttt
Arg Ala Pro Lys Ala Thr Ala Pro Thr Glu Leu Asn Cys Asp Asp Phe
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							gat Asp									390
							aaa Lys									438
							999 Gly 140									486
							cca Pro									534
							cta Leu						tagg	gtgct	igt	583
ccto	ette	ett d	cttag	ggtgg	gg ag	gcctt	ggaa	a gga	aatta	aatt	ctto	gcttt	at g	gtgaa	aatgga	643
atacccagtt actgcccact aatatgaaaa agctaattat agtctctgaa actggatcag													703			
atta	acttt	igg t	ggtt	caaga	at c	ttca	aatct	at!	gct	gctt	tgta	at				748
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					_		ttg Leu	_		_						102
							gaa Glu									150
							tgt Cys									198

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_		_			atg Met											246
	_	_		_	gca Ala			_	_		_				_	294
	_		_	_	act Thr 90	_				_		_	_	_		342
					gat Asp											390
					gat Asp											438
_	_				aaa Lys							_				486
					agt Ser											534
					aat Asn 170											582
					gat Asp		_	_				_	_	_	_	630
_	_		_		tta Leu		_	_	_		_	_	_			678
		_		_	cga Arg		_	-	_			_	_			726
_				_	aat Asn					_				_	_	774
					gac Asp 250											822
_	_	_			aag Lys		_				_		_			870

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_		_			_	-	_			_		aga Arg	_	918
			_	_				_	_	_		gga Gly		966
												G1 Y 999		1014
_			_	_		_	_	_				gca Ala		1062
												aga Arg 355		1110
												cga Arg		1158
	 					_	_	_			_	cct Pro		1206
-		_										tgt Cys		1254
												ggc Gly		1302
												gag Glu 435		1350
												tgc Cys		1398
												ggc Gly		1446
												gca Ala		1494
												ttt Phe		1542

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	caa Gln														1590
_	cgt Arg		_			_				_	_	-			1638
_	agt Ser				_	_	-	-	_						1686
_	aaa Lys 550		_		_	_		_	_	_	-	_	_	_	1734
	ctg Leu														1782
	acc Thr														1830
	aac Asn														1878
	aaa Lys														1926
	gag Glu 630														1974
	tgc Cys														2022
	ggc Gly	_	_	-	_	_	_	_	_		_		-		2070
	gaa Glu														2118
	ggt Gly														2166
	tat Tyr 710														2214

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agt gat cct Ser Asp Pro 725	gta cgt Val Arg	gat gct Asp Ala 730	gat gg Asp Gl	ıc aaa y Lys	tcg Ser 735	tac Tyr	aac Asn	aat Asn	cag Gln	tgt Cys 740	2262
acc atg tgt Thr Met Cys											2310
tat tct cgc Tyr Ser Arg	tcc aga Ser Arg 760	tca aat Ser Asn	ggg ac Gly Th 76	ır Gly	tca Ser	gaa Glu	tca Ser	999 Gly 770	aag Lys	gat Asp	2358
aca tgt gat Thr Cys Asp 775	gag ttt Glu Phe	aga agc Arg Ser	caa at Gln Me 780	g aaa et Lys	aat Asn	gga Gly	aaa Lys 785	ctt Leu	atc Ile	tgc Cys	2406
act cga gaa Thr Arg Glu 790	agt gac Ser Asp	cct gtc Pro Val 795	cgg gg Arg Gl	gt cca .y Pro	gat Asp	ggc Gly 800	aag Lys	aca Thr	cat His	ggt Gly	2454
aat aag tgt Asn Lys Cys 805	act atg Thr Met	tgt aag Cys Lys 810	gaa aa Glu Ly	aa ctg ⁄s Leu	gaa Glu 815	agg Arg	gaa Glu	gca Ala	gct Ala	gaa Glu 820	2502
aaa aaa aga Lys Lys Arg	aag agg Lys Arg 825	atg aag Met Lys	aca gg Thr Gl	ga gca Ly Ala 830	ata Ile	cag Gln	gag Glu	aaa Lys	gga Gly 835	gca Ala	2550
ata cag gag Ile Gln Glu	aaa gga Lys Gly 840	gca atg Ala Met	aca aa Thr Ly 84	s Arg	atc Ile	tgt Cys	gtc Val	gtg Val 850	aat Asn	ttc Phe	2598
gaa gca tgc Glu Ala Cys 855	aga gaa Arg Glu	atg gaa Met Glu	agc tt Ser Le 860	ta tct eu Ser	gca Ala	cca Pro	gag Glu 865	aaa Lys	ata Ile	acc Thr	2646
ctg ttc gag Leu Phe Glu 870	gcc cat Ala His	atg gca Met Ala 875	Arg Cy	gc aca ys Thr	tca Ser	ata Ile 880	aat Asn	gtg Val	cta Leu	tgt Cys	2694
gtc aga gca Val Arg Ala 885	tct ttg Ser Leu	atc gag Ile Glu 890	aag ct . Lys Le	ta atg eu Met	aaa Lys 895	gaa Glu	aaa Lys	aga Arg	aag Lys	atg Met 900	2742
aag aga aat Lys Arg Asn	caa gta Gln Val 905	Ala Ser	cct ca Pro Gl	aa ata ln Ile 910	atg Met	caa Gln	agg Arg	atg Met	agt Ser 915	gca Ala	2790
gtg aat ttc Val Asn Phe			.ggaacaa	a tgaa	ctcat	ic to	gecet	taga	3		2838
agaatgaccc	agtgcacg	gt gctga	itggaa a	agttct	atac	aaa	caag	tgc '	tacai	tgtgca	2898
gagctgtctt	tctaacag	aa gcttt	.ggaaa g	gggcaa	agct	tcaa	agaa	aaa (	ccat	cccatg	2958
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<400> 7
His Glu Phe Gln Ala Phe Met Lys Asn Gly Lys Leu Phe
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Ser Glu Tyr Arg Lys Ser Arg Lys Asn Gly Arg Leu Phe
<210> 9
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Asp Asp Phe Lys Lys Gly Glu Arg Asp Gly Asp Phe Ile
<210> 10
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Ser Glu Phe Arg Asp Gln Val Arg Asn Gly Thr Leu Ile
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Ser Ala Phe Arg Pro Phe Val Arg Asn Gly Arg Leu Gly
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Ser Glu Tyr Arg His Tyr Val Arg Asn Gly Arg Leu Pro
                  5
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Asp Glu Phe Arg Arg Leu Leu Gln Asn Gly Lys Leu Phe
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Ser Gln Tyr Gln Asn Gln Ala Lys Asn Gly Ile Leu Phe
                  5
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<210> 16
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<212> PRT
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Ala Glu Tyr Arg Glu Gln Met Lys Asn Gly Arg Leu Ser
 1
                  5
<210> 17
<211> 13
<212> PRT
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<223> Description of Unknown Organism: Serine protease
      inhibitor
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Asn Glu Tyr Arg Lys Leu Val Arg Asn Gly Lys Leu Ala
<210> 18
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Asp Glu Phe Arg Ser Gln Met Lys Asn Gly Lys Leu Ile
                 5
<210> 19
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Pro Gln Asp Lys Lys Phe Phe Gln Ser Leu Asp Gly Ile Met Phe Ile
Asn Lys
<210> 20
<211> 18
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Thr Arg Glu Asn Asp Pro Ile Gln Gly Pro Asp Gly Lys Met His Gly
                                     10
Asn Thr
<210> 21
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<400> 21
Thr Arg Glu Asn Asp Pro Val Leu Gly Pro Asp Gly Lys Thr His Gly
Asn Lys
<210> 22
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<212> PRT
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<400> 22
Thr Arg Glu His Asn Pro Val Arg Gly Pro Asp Gly Lys Met His Gly
                                     10
Asn Lys
<210> 23
<211> 18
<212> PRT
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Thr Arg Glu Ser Asp Pro Val Arg Gly Pro Asp Gly Arg Met His Gly
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Asn Lys
<210> 24
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<400> 24
Thr Arg Glu Asn Asp Pro Ile Glu Gly Leu Asp Gly Lys Ile His Gly
Asn Thr
<210> 25
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Thr Arg Glu Asn Asp Pro Ile Arg Gly Pro Asp Gly Lys Met His Gly
Asn Leu
<210> 26
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                                     10
Asn Lys
<210> 27
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<400> 27
Thr Arg Glu Asn Asp Pro Ile Gln Gly Pro Asp Gly Lys Val His Gly
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Asn Thr
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<210> 28
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Thr Arg Glu Ser Asp Pro Val Arg Asp Ala Asp Gly Lys Ser Tyr Asn
Asn Gln
<210> 29
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Thr Arg Glu Ser Asp Pro Val Arg Gly Pro Asp Gly Lys Thr His Gly
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Gln Asp Lys Lys Phe Phe Gln Ser Leu Asp Gly Ile Met Phe Ile Asn
Lys Cys Ala Thr Cys
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<211> 37

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Cys Asp Asp Phe Lys Lys Gly Glu Arg Asp Gly Asp Phe Ile Cys Pro
Asp Tyr Tyr Glu Ala Val Cys Gly Thr Asp Gly Lys Thr Tyr Asp Asn
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Arg Cys Ala Leu Cys
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Cys Ser Ala Phe Arg Pro Phe Val Arg Asn Gly Arg Leu Gly Cys Thr
Arg Glu Asn Asp Pro Val Leu Gly Pro Asp Gly Lys Thr His Gly Asn
                                 25
Lys Cys Ala Met Cys
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<400> 33
Cys Lys Glu Tyr Glu Lys Gln Val Arg Asn Gly Arg Leu Phe Cys Thr
Arg Glu Ser Asp Pro Val Arg Gly Pro Asp Gly Arg Met His Gly Asn
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Lys Cys Ala Leu Cys 35

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<400> 34
Cys Ser Gln Tyr Gln Asn Gln Ala Lys Asn Gly Ile Leu Phe Cys Thr
Arg Glu Asn Asp Pro Ile Arg Gly Pro Asp Gly Lys Met His Gly Asn
                                 25
Leu Cys Ser Met Cys
        35
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      inhibitor
<400> 35
Cys Asn Glu Tyr Arg Lys Leu Val Arg Asn Gly Lys Leu Ala Cys Thr
Arg Glu Asn Asp Pro Ile Gln Gly Pro Asp Gly Lys Val His Gly Asn
                                 25
Thr Cys Ser Met Cys
        35
<210> 36
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      inhibitor
<400> 36
Cys Ser Glu Tyr Arg Lys Ser Arg Lys Asn Gly Arg Leu Phe Cys Thr
Arg Glu Asn Asp Pro Ile Gln Gly Pro Asp Gly Lys Met His Gly Asn
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Thr Cys Ser Met Cys
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inhibitor

<400s 37

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Arg Glu His Asn Pro Val Arg Gly Pro Asp Gly Lys Met His Gly Asn 20  $\phantom{-}25\phantom{+}30\phantom{+}$ 

Lys Cys Ala Met Cys 35

<210> 38

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<223> Description of Unknown Organism: Serine protease inhibitor

<400> 38

Cys Ser Glu Tyr Arg His Tyr Val Arg Asn Gly Arg Leu Pro Cys Thr 1 10 15

Arg Glu Asn Asp Pro Ile Glu Gly Leu Asp Gly Lys Ile His Gly Asn 20 25 30

Thr Cys Ser Met Cys 35

<210> 39

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Cys Asp Glu Phe Arg Arg Leu Leu Gln Asn Gly Lys Leu Phe Cys Thr 1 5 10 15

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Lys Cys Ala Met Cys 35

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<111> 37

<212> PRT

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<223> Description of Unknown Organism: Serine protease inhibitor

<400> 40

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Gln Cys Thr Met Cys 35

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<223> Description of Unknown Organism: Serine protease
 inhibitor

<400> 41

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Lys Cys Thr Met Cys 35